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Disease-a-Month

Cerebral Vascular Disease

JOSEPH M. FOLEY
SIMON HORENSTEIN

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THE PROBLEMS of cerebral vascular disease, so long ignored by so many, have in recent years been attracting increasing attention from practitioners and investigators.

The first reason for this awakening interest is that the practicing physician finds cerebral vascular disease occupying a larger part of his practice. Paradoxically, this is because he is a better physician with better tools than his forebears. As he cures infections, controls diabetes and manages heart disease more effectively more patients survive to develop cerebral vascular disease.

Secondly, the physiologist and the physiologically minded clinical investigator have developed new technics of research which have provided a more dynamic orientation to the problems of vascular disease in general and cerebral vascular disease in particular. Introduction of the nitrous oxide method for studying cerebral blood flow (1) and the polarographic method of studying oxygen availability in the brain and its application both to collateral circulation and experimental cerebral infarction (2, 3) are examples of this increasingly productive physiologic trend.

Thirdly, during the past 20 years clinicians and pathologists have shown an increasing interest in the correlation of clinical events and pathologic findings. The syndromes of basilar (4) and carotid (5) artery disease have been clarified. Angiographic visualization of the cerebral vessels, introduced by Moniz (6) in 1931, has permitted a better delineation and understanding of aneurysms and angiomas. A renewed interest in the mutual problems of neurology and internal medicine has yielded important information about the relation of cerebral vascular disease to vascular disease in other parts of the body. The concepts of the *cerebral hemodynamic crisis* (7) and *cerebral vascular insufficiency* (8) have been developed to clarify many things and to stimulate further work in the pathogenesis of ischemic cerebral vascular disease.

Lastly, there have been efforts at prevention and treatment, and even those physicians who are not awakened to interest by the exciting new knowledge of physiology and pathology bestir themselves to action at the prospect that, after all, something might be accomplished for the patient out of all this. The surgical attack on aneurysms and angiomas, the use of stellate ganglion block and chemical autonomic blockade, the use of vasodilators, the administration of hypotensive agents and the use of anticoagulants are a few examples of the therapeutic efforts of recent years. Halting and fumbling as some of these may be, and controversial as others may be, there is no doubt that they have been responsible in large part for the awakening of widespread interest in cerebral vascular disease.

The whole area of cerebral vascular disease obviously cannot be covered in a treatise of this sort. We have chosen rather to emphasize some anatomic, physiologic and pathologic data which are important and which might be forgotten, and to call to attention certain clinical data regarding diagnosis and treatment.

Anoxic encephalopathy has been treated in some detail because its prevention lies in the hands of practitioners whose task may be made easier by some understanding of its mechanisms and effects.

Hypertensive and arteriosclerotic vascular disease have occupied most of our attention and this is as it should be, since these are the most common causes of neurologic disability. Aneurysms and angiomas have been subject to intense interest and controversy in recent years and we have tried to present a point of view about their management. Venous disease is far

less frequent than arterial disease, but presents certain problems which we considered worthy of some clarification. Finally, we have included some directions on the practical management of the patient with a neurologic deficit following a vascular lesion of the brain.

ANATOMIC CONSIDERATIONS

Starting at the arch of the aorta, the circulatory supply of the brain is protected by collaterals against occlusion. The blood supply of the brain comes entirely from the internal carotid and vertebral arteries, the external carotids in man normally contributing nothing.

The internal carotid arises on each side from the bifurcation of the common carotid artery, at the upper level of thyroid cartilage. As it ascends through the neck, it is vulnerable to trauma, especially penetrating trauma, and thrombi on the traumatized endothelium may provide the mechanism for occlusion or the origin for emboli, resulting in the confusing picture of delayed cerebral disorder following injury to the neck (9). Trauma in this location leading to a carotid-jugular fistula can compromise the blood supply to a hemisphere. Ascending through the neck, the internal carotid gives no branches but enters the petrous portion of the temporal bone, in which it makes an S-shaped curve, passing through the cavernous sinus and entering the subarachnoid space medial to the anterior clinoids. This arrangement in relation to the cavernous sinus allows the formation of a carotid-cavernous shunt with pulsating exophthalmos in trauma or in "spontaneous" rupture of the vessel due to aneurysm.

The ophthalmic artery is given off during the passage through the cavernous sinus. It supplies the optic nerve, the globe of the eye and the other soft tissues of the orbit, where there is an anastomotic connection with the external carotid system. In some cases of internal carotid artery occlusion, this nasociliary anastomotic channel becomes functional and helps to provide blood flow to the ipsilateral hemisphere. This accounts for the exophthalmos sometimes seen after occlusion of the internal carotid. After entering the subarachnoid space, the carotid divides into the posterior communicating artery, the middle cerebral artery and the anterior cerebral artery. The anterior communicating artery, connecting the two anterior cerebrals, then forms the anterior boundary of the circle of Willis.

The vertebral artery arises on each side as the first branch of the subclavian. It has the same directness of purpose as the internal carotid, giving off no significant branches in the lower neck. It passes through the transverse processes of the upper 6 cervical vertebrae, winding around the atlas to form a siphon rather like that formed by the internal carotid in the petrous portion of the temporal bone. These siphons probably have the purpose of protecting against sudden postural change. The vertebral artery in the neck is vulnerable to trauma in the same manner as the carotid. Having penetrated the dura just above the foramen magnum, the vertebral arteries from each side fuse at the junction of the pons and medulla to form the basilar artery, which continues along the base of the pons to divide at the tentorial opening into the posterior cerebral arteries, which form the posterior part of the circle of Willis. The "circle" is closed by the posterior communicating arteries, which run from the posterior cerebrals to the internal carotids.

From the arteries at the base of the brain, there is a relatively uniform plan of branching (10):

1. Short penetrating branches, arising at approximately right angles from a main trunk, supply the midline and the basal structures. Such are the lenticulostriate arteries, a cluster of vessels which arise from the middle cerebral arteries, to supply the putamen, internal capsule, caudate and anterior thalamus, and the thalamoperforating branches from the posterior cerebral arteries, which supply the posterior thalamic nuclei. In such vessels there are relatively few anastomotic channels, and they are closer to being "end-arteries" than other vessels in the brain. This deficiency may explain in part the special vulnerability of some of these areas to infarction.

2. Short circumferential arteries are continuations of the main trunk and supply the lateral basal parts of the cerebral hemisphere and the lateral parts of the medulla, pons and midbrain. These vessels may have generous anastomoses with one another in the pia.

3. Long circumferential arteries are also continuations of the main trunk. They supply the cerebellum and the convexity of the cerebral cortex. Anatomic studies by Vander Eecken and Adams (11) have demonstrated abundant pial communications between such vessels, so that there are anastomoses between the anterior, middle and posterior cerebral arteries. There do not seem to be any effective anastomoses, except through main trunks, between the infratentorial and supratentorial arteries.

Figure 1 illustrates the classic outline of the circle of Willis and its branches and the table shows the distribution of supply and the clinical consequences of infarction in these various arterial distributions.

Some interesting and important effects on blood vessels are produced by the herniations which occur as a consequence of increased intracranial pressure. In herniation of the temporal lobe through the incisura of the tentorium, a posterior cerebral

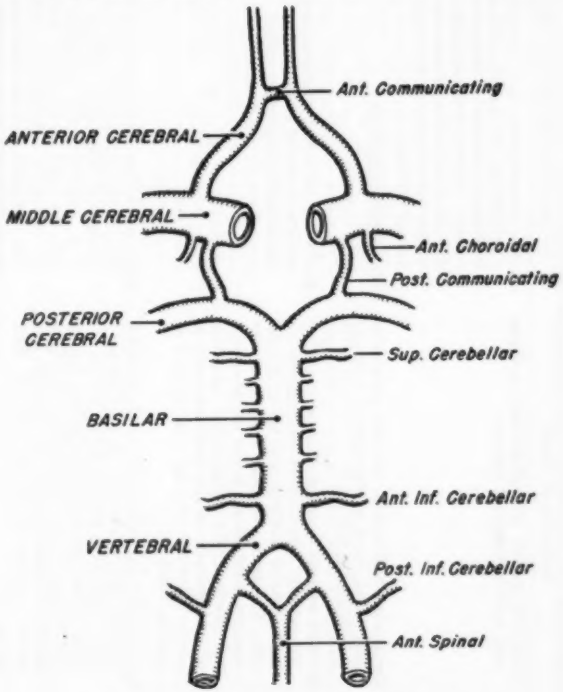

FIG. 1.—The arterial supply of the brain.

artery may be compressed against the firm free edge of the tentorium, producing a falsely localizing hemianopia (12). In herniation of the cingulate gyrus under the falx cerebri, the anterior cerebral arteries and their branches lie in such close proximity to the free edge of the falx that infarcts may occur in the anterior cerebral supply to confuse the clinical picture (13).

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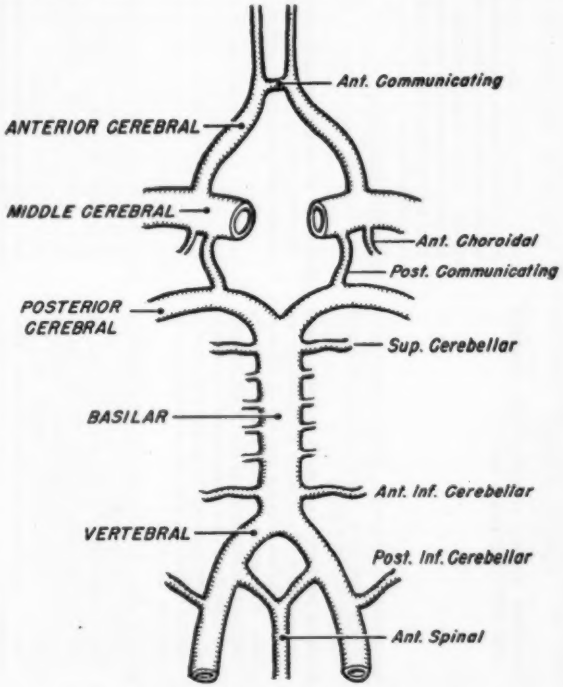

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Distribution of Supply and Consequences of Infarction

Artery	Territory of Supply	Symptoms Arising from Occlusion
Internal carotid	Combined supply of ophthalmic, anterior and middle cerebral arteries	Acute—unconsciousness, complete loss of function of the opposite side of the body, ipsilateral blindness, frequently fatal Chronic—intermittent episodes of loss of function with subtotal recovery, especially monocular blindness, faciobrachial or crural monoplegia
Ophthalmic	Optic nerve and retina; the fat, connective tissue, and bone of the orbital wall and extraocular muscles	Monocular blindness
Anterior cerebral	Anterior part of anterior limb of the internal capsule (Heubner's perforating artery), orbital surface and tip of frontal lobe, the entire mesial surface of the cerebral hemisphere to the parieto-occipital junction, the parasagittal convexity of the hemisphere, the ipsilateral part of corpus callosum and the anterior part of caudate nucleus	Early loss of consciousness, confusion, contralateral crural monoplegia, contralateral crural cortical sensory defect
Middle cerebral	Sparing that part supplied by the anterior cerebral artery, the convexity of the cerebral hemisphere and its white matter, including the lateral orbital frontal region and temporal tip. Perforating branches supply internal capsule, caudate and lenticular nucleus and the anterior thalamus	Total infarction—a syndrome much like that of the internal carotid save for absence of unilateral blindness. Deficit usually severe, complex and permanent. Aphasia, agnosia, apraxia when the lesion involves the dominant hemisphere. Cortical sensory loss common. Usual syndromes incomplete. Although many variants, most common is faciobrachial monoplegia. If the lesion is of dominant hemisphere, patient aphasic to some degree

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DISTRIBUTION OF SUPPLY AND CONSEQUENCES OF INFARCTION (*Cont.*)

ARTERY	TERRITORY OF SUPPLY	SYMPTOMS ARISING FROM OCCLUSION
Posterior cerebral	Midbrain, superior cerebellar peduncle, posterior part of thalamus, including lateral geniculate body, posterior part of internal capsule, the base and posterior ⅔ of temporal lobe, splenium of corpus callosum and medial surface of occipital lobe	Total infarction infrequent. Infarction adjacent to or involving subthalamic nucleus — contralateral hemiballismus resulting from occlusion of perforating thalamic branch. Occlusion of thalamo-geniculate branch with infarction of thalamus and lateral geniculate body—contralateral hemianopia and hemianesthesia. Occlusion of calcarine branches—quadrantanopia or hemianopia. Occlusion of branch to basis pedunculi—ipsilateral 3d nerve palsy and contralateral hemiplegia, with or without contralateral tremor
Vertebral-basilar	The structures of the posterior fossa (pons, medulla, cerebellum) below bifurcation of basilar into posterior cerebral arteries	Diagnostic criteria of disease in this system: (1) signs of abnormality involving 3d-12th cranial nerves in any combination, 3d, 6th, 7th, most commonly, (2) cerebellar dysfunction and (3) long tract signs especially corticospinal. Chronic occlusive syndrome resembles that of carotid save for distribution of neurologic deficit. Extensive infarction less common than patchy infarction, complete transverse bulbar infarction incompatible with survival
Paramedian	Paramedian base of pons and midbrain, ventral pontine tegmentum	Paralysis of 3d, 4th, 6th cranial nerve ipsilateral to the occlusion with contralateral hemiplegia

DISTRIBUTION OF SUPPLY AND CONSEQUENCES OF INFARCTION (*Cont.*)

ARTERY	TERRITORY OF SUPPLY	SYMPTOMS ARISING FROM OCCLUSION
Short circumferential	Lateral base and medial tegmentum of pons and midbrain	Ipsilateral 5th or 7th cranial nerve paralysis and cerebellar ataxia. Contralateral disturbance of position and vibration senses
Long circumferential		
Superior cerebellar	Lateral tegmentum of midbrain, upper pons and cerebellum, brachium conjunctivum, brachium pontis, superior cerebellum, roof nuclei of cerebellum, lateral spinothalamic tract, descending pupillodilator fibers	Ipsilateral Horner's syndrome and cerebellar ataxia. Contralateral disturbance of pain and temperature sensation on face, arm and leg
Middle cerebellar	Anterior inferior cerebellum, lateral tegmentum of pons and upper medulla, middle and inferior cerebellar peduncles, descending pupillodilator fibers, nuclei of 5th, 7th, 8th cranial nerves, lateral spinothalamic tract	Ipsilateral cerebellar ataxia, loss of touch, pain and temperature on face, Horner's syndrome, deafness, facial paralysis, nystagmus and vertigo. Contralateral disturbance of pain and temperature on arm, trunk, leg
Posterior, inferior cerebellar	Posterior, inferior cerebellum, lateral medullary tegmentum including descending pupillodilator fibers, vestibular nuclei, spinal nucleus of trigeminal nerve, 9th-10th cranial nerve nuclei, inferior cerebellar peduncle, dorsal spinocerebellar tract, lateral spinothalamic tract	Ipsilateral Horner's syndrome, dizziness, nystagmus, decreased pain and temperature sensation on face, cerebellar ataxia, weakness of soft palate, vocal cord with dysphagia and dysphonia. Reduced pain and temperature sensation on contralateral arm, trunk, leg

There are many anomalies of the circle of Willis, and some of them probably have importance in the distribution of infarcts. It is not uncommon to find one vertebral artery a tiny thread while the other is of the same caliber as the basilar, but hypoplasia of an internal carotid is rare. Sometimes both anterior cerebral arteries are supplied from the carotid of one side, or the anterior cerebral arteries may fuse into a single vessel beyond the anterior communicating artery. A common anomaly is hypoplasia of one or both posterior cerebral arteries, always compensated for by large posterior communicating arteries, so that the entire supply of a hemisphere arises from the internal carotid artery. Variations are common in the vertebral-basilar branches. A posterior inferior cerebellar artery may be absent on one side, compensated for by a large anterior inferior cerebellar artery which takes over its supply. The number of possible anomalies is unlimited, but there is always an anatomic compensation, and no area of the brain is left in a critical state by an anomaly unless disease of the vessels complicates the picture.

The arteries of the brain have one important histologic difference from those elsewhere, in that they lack an external elastic lamina. The capillary density of any area of the brain can generally be correlated with cellular density, synaptic surface and metabolic activity. Thus, gray matter has a much denser capillary network than white matter. Certain specific nuclei, such as the nucleus supraopticus and nucleus paraventicularis of the hypothalamus, with high metabolic demand and dense neuronal population, have the densest capillary network of any structures in the nervous system (14).

The venous drainage of the brain is complex. A matter of important practical concern is that almost all the venous blood from the brain leaves the skull through the internal jugular veins and the largest part of the contribution to the internal jugular vein is from the lateral sinus. When one lateral sinus or one jugular vein is occluded by disease or surgical operation (as in radical neck dissection for malignancy), the venous channels of the other side are usually able to compensate. But in some cases there is anomalous failure of development of one lateral sinus, so that if the opposite one is occluded, obstruction to venous outflow produces the syndrome of benign intracranial hypertension, papilledema without focal neurologic symptoms or signs, because of the inactivation of the resorptive properties of the pacchionian granulations in the dural sinuses. A like effect may be produced in thrombosis of the superior vena cava.

PHYSIOLOGIC CONSIDERATIONS

The most important physiologic consideration in the understanding of vascular disease of the brain is the enormous oxygen requirement of nervous tissue. The brain represents only 2% of the body weight, yet requires one sixth of the cardiac output and utilizes 20% of the total oxygen consumption of the body at rest (15). Anatomically, this high demand is a function of the nerve cell, and particularly of the cell body and the synaptic connections. Deprived totally of oxygen for a few seconds, the nerve cell ceases to function; if total deprivation lasts 4-5 minutes, the nerve cell dies. The fate of a given nerve cell when exposed to reduced oxygenation is a function of the intensity and duration of the hypoxic insult at the cell level. In incomplete hypoxia, the nerve cell may be functionless for hours or days but still may be able to regain normal function.

Enormous impetus has been given to the study of the physiology of the cerebral circulation by the introduction and development of a satisfactory method of determining cerebral blood flow. This method, developed by Kety and Schmidt (1), is complicated in its theory and execution. While it is by no means a routine procedure, the limitations of the method are understood and a large body of experiments have been carried out intelligently through its use (16). It utilizes nitrous oxide, which has the advantage of being both metabolically inert and freely diffusible. Blood is sampled from the carotid artery and the jugular vein, and by application of the Fick principle the rate of cerebral blood flow is determined.

The nitrous oxide method is applicable to man with little inconvenience to the subject. However, since the calculations are based on an assumed average brain weight and nitrous oxide diffusion coefficient, the results are applicable to large samples rather than to a single person. The problem of averaging samples also complicates the newer labeled red cell method (17). These methods reveal information about the whole brain circulatory function over relatively long periods (several minutes) and cannot disclose either rapid changes or regional variations. Those who have applied the nitrous oxide method to the study of cerebral circulatory physiology have been careful to keep these limitations in mind, and parallel work done in several different laboratories has yielded remarkably similar results.

The electropolarographic method (EPG) measures oxygen availability in the brain. It has the advantage of recording rapid

changes and local variations. Unlike the nitrous oxide method which requires averaging of many samples from many persons, the method of EPG permits comparative study of various portions of the brain in the same subject. It is chiefly a qualitative method, since the diffusion coefficient of oxygen in the brain is not yet known. Further, it requires craniotomy and involves the introduction of recording electrodes into or onto brain surface and, therefore, its use in man is sharply limited. In the experimental animal it has given much useful information about collateral cerebral circulation and about the dynamics of cerebral infarction and trauma (18, 19). With a rather different technic, oxygen availability in anemia (20), during convulsions (21), and after electrical stimulation (22) was studied by earlier workers.

Cerebral blood flow depends on 2 factors: the pressure gradient across the capillary net between the arteries and the veins, and the cerebral vascular resistance, which is the result of a large number of variables, both normal and pathologic. It has been made clear in recent years that the cerebral circulation does not follow passively on changes in systemic blood pressure (15). Indeed, if it did, the vulnerable nerve cells would be taxed many times beyond their capacity for survival. There are a whole host of complex reflex and homeostatic mechanisms which prevent the circulation of the brain from passively following the systemic blood pressure. Most of these mechanisms are designed to alter cerebral vascular resistance. In the normal young adult, a systolic blood pressure of 70 mm. Hg appears to be critical for the brain. Above this figure cerebral blood flow is adequately maintained; below this figure symptoms and signs of hypoxia appear. It should be emphasized, however, that this figure of 70 mm. Hg applies only to normal young adults. Disease of the vessels changes the situation completely, the homeostatic mechanisms no longer being normal. Thus, the hypertensive patient with a customary systolic blood pressure of 250 mm. Hg may develop severe brain destruction during a surgical procedure in which his blood pressure is allowed to stay for any period in the neighborhood of the traditionally normal 120.

The matter of "spasm" in cerebral blood vessels is still of concern to the practitioner not working in the field, and it has been confused in recent years by contradictory studies on the value of stellate ganglion block in vascular occlusion of the brain. The facts about "spasm" of cerebral blood vessels might be stated as follows:

1. Spasm can occur in the blood vessels of the brain in response to nonphysiologic stimuli. Electrical stimulation or direct percussion of an exposed pial vessel can produce blanching of the cortex over a wide area. A similar dramatic blanching of cortex, with infarction, can be produced by the injection of saline under pressure into a pial vein (3).

2. It is possible to demonstrate nerves in the blood vessels of the brain, especially in the adventitia of large vessels and in smaller branches in the parieto-occipital region.

3. Constriction of cerebral vessels can be produced by stimulation of the sympathetic ganglia, but it is a weak and feeble response, about ⅛ of the response attainable from extracranial vessels.

4. Blocking the stellate ganglion in man produces no alteration in cerebral vascular resistance or cerebral blood flow (23).

5. The spasm produced in cerebral vessels by percussion or electrical stimulation or distention of a vein and the subsequent infarct cannot be prevented by prior blocking or excision of the cervical sympathetic ganglia (3).

6. High arterial intraluminal pressure especially if maintained, as in the experiments of Byrom with hypertensive encephalopathy (31), produces localized constrictions in small blood vessel walls.

On the basis of these facts, it would appear that autonomic control of cerebral vessels is not an important regulatory mechanism, and that the blocking of sympathetic ganglia has no rationale in disease of cerebral blood vessels.

The influence of chemical and pharmacologic agents on cerebral blood flow and vascular resistance is of considerable practical importance. It is fallacious to equate vasodilatation with blood flow, for although vasodilatation may reduce cerebral vascular resistance, blood flow depends also on the pressure gradient between the arteries and the veins. An agent such as histamine, which dilates the cerebral vessels and also dilates the systemic vessels to the same degree, produces no improvement of cerebral blood flow since there is a concomitant drop in systolic blood pressure. Some agents, like aminophylline, which may dilate the coronaries, constrict the brain vessels, increasing cerebral vascular resistance at the same time they produce only a slight rise in blood pressure, so that cerebral blood flow is either reduced or unchanged. Other agents, like alcohol and nicotinic acid, produce a cutaneous flush but make no difference to either cerebral blood flow or cerebral vascular resistance. Papaverine has at least a theoretical advantage in that it can produce vasodilatation of cerebral vessels without a negating associated drop in systemic blood pressure (15).

The most effective vasodilator of the cerebral vessels is carbon dioxide, and since it does not produce any drop in blood pressure

by significant systemic vasodilatation, it can increase cerebral blood flow. Low oxygen tension has the same capacity as high carbon dioxide tension, producing vasodilatation and increased blood flow. Conversely, low carbon dioxide tension and extremely high oxygen tension increase cerebral vascular resistance and reduce cerebral blood flow. These metabolites of tissue respiration are probably as available as possible under conditions of ischemia; exogenous administration of carbon dioxide is therefore not indicated in the management of ischemic disease of the brain.

INFARCTS OF THE BRAIN

An infarct is a zone of necrosis which results when a localized area is deprived of blood. Generally, infarcts occur in the territory of a given blood vessel, but sometimes they occupy the overlapping distribution of 2 or 3 vessels. The mechanisms of infarction are still not completely understood, and there are many areas of controversy, but enough is known to formulate some principles for proper management of the patient who has suffered a cerebral infarct.

Embolic occlusion of a cerebral blood vessel with consequent infarction is a mechanism relatively easy to understand. A particle coming from elsewhere lodges suddenly in an artery, the collateral circulation does not become effective and the tissue in the distribution of the occluded vessel undergoes necrosis.

Emboli arise most commonly from the heart, either from mural thrombi in myocardial infarction, from auricular thrombi in fibrillation and, more rarely in recent years, from vegetations on the valves in septic or aseptic endocarditis. The paradoxic embolus, from leg vein to brain artery through a patent interventricular septum, is the sort of thing all books mention but few people see. Ulcerations and thrombi in the great vessels of the neck constitute sources for emboli which are often overlooked at autopsy. Sometimes an atheromatous plaque itself may be the embolic particle. Fat emboli from broken bones in the elderly may produce severe cerebral effects. Even amniotic fluid emboli have occurred in the brain.

The frequency of embolic occlusion to brain vessels has usually been underestimated. In careful studies in recent years, Fisher and Adams (24) have emphasized emboli as a cause. In their series at the Boston City Hospital in 1949, 129 cases of cerebral infarction came to autopsy. They reported that 57 of

these cases (44%) were caused by emboli, while only 21 cases (16%) were caused by thrombosis of a large artery.

Thrombosis within the lumen of a vessel is a facile explanation for many cases of infarction. In some instances, it is a perfectly provable cause, as in the arteritides, especially those which occur in vessels not significantly affected by atherosclerosis. There can be no doubt either, that thrombi may form in atherosclerotic vessels, although the suggested mechanisms of initiation of the thrombus (slowing of the stream, eddying, rupture of an atheromatous plaque, generalized or localized hypercoagulability of the blood) are difficult to prove in any case. The certain fact is that with the possible exception of severe polycythemia vera thrombi do not form in normal brain arteries. The largest number of vessels in which thrombi form are already narrowed or occluded by atherosclerosis. In many cases of cerebral infarction it is not possible to find a complete occlusion of the appropriate vessel. In old lesions, recanalization or thrombus resorption may have occurred. In emboli, the plug in the large vessel may have moved on into smaller ones. In some cases of localized infarction within the middle cerebral or anterior cerebral arterial distribution, the occlusion may be in the internal carotid artery. Yet, when all these possibilities are taken into account, there remain some cases in which infarction has occurred in cerebral atherosclerosis without complete occlusion of any one vessel. This has led some to argue that the cause must have been spasm in the appropriate vessel. It is dangerous logic to argue to a positive conclusion on the basis of negative data; and the concept of spasm as a cause of infarcts in the brain no longer can be taken seriously.

It has already been pointed out that the sudden complete occlusion of a vessel by embolus results in infarction in the supply of the occluded vessel. On the other hand, gradually produced total occlusion of a vessel does not necessarily produce infarction. When the patency of any vessel is reduced below a critical level, the structural integrity of the tissue supplied by that vessel becomes dependent on the restitution of blood flow through the collaterals, which, to prevent infarction, must take over in a matter of seconds or minutes. It has been demonstrated in the monkey, using the polarographic method, that collateral response occurs in a matter of seconds after deprivation of blood to a localized area. The collaterals are enabled to respond by the simple establishment of a pressure differential. Before the vessel is occluded, the perfusion pressure is the same as in the

collaterals and so there is no gradient by which flow can occur into the area. But when the vessel is occluded, there is distal to the point of occlusion a pressure drop which results in a pressure difference, a gradient between the collaterals and the threatened area, which allows blood to move from the collaterals to restore blood flow.

Thus, in every occlusion (or in every significant stenosis) of a vessel there is a period of crisis, called by Denny-Brown the *cerebral hemodynamic crisis* (7). A crisis is defined by the Oxford English Dictionary as "a state of affairs in which a decisive change for better or worse is imminent." The decisive change which is impending in this state of things depends on the collaterals. If they are effective, the tissue survives. If they are ineffective, an infarct occurs. An incomplete infarct in terms of the site of the vascular occlusion may occur when there is an incomplete success by the collateral circulation. Thus an occlusion in the most proximal part of the middle cerebral artery may produce infarction in the total distribution of the vessel, infarction in the distribution of the penetrating branches only or no infarction at all.

The term "insufficiency" was applied to the cerebral vascular system originally by Denny-Brown (8) to signify an abnormal physiologic state consequent on chronic occlusion or stenosis of a major cerebral artery. Carotid or basilar insufficiency is a continuing potential state, and the cerebral hemodynamic crisis is its intermittent consequence. The cerebral hemodynamic crisis makes its appearance as an effect of various factors, among which are reduced systolic pressure, increased tissue demand and anoxia. Insufficiency, then, is a state which is recognized only by the appearance of hemodynamic crises.

A variant on this pattern of reaction arises in those conditions in which an occlusion has occurred and in which the collaterals have become effective. This has been studied best in chronic occlusion or chronic severe stenoses of the internal carotid artery. On the basis of arteriographic and pathologic studies it is known that such occlusions or stenoses may be present for many years without producing a neurologic deficit. A common example is the patient who has had a ligation of the internal carotid artery for aneurysm of the circle of Willis. With the passage of time, however, the new-found arrangement may become *insufficient*. This *insufficiency* may be altered by the drastic solution of infarction, or the result may be a repeated series of hemodynamic crises in which function is lost for a matter of seconds,

minutes or even hours, to be regained once again, with little or no residual deficit.

It is generally accepted, following Denny-Brown (7), that alterations in the state of general circulation are responsible for many such recurrent episodes. One sees patients, for example, with chronic internal carotid occlusion who are asymptomatic until they have a blood pressure drop, as with a myocardial infarct, a bleeding peptic ulcer or spinal anesthesia. Then symptoms of a deficit in the distribution of the occluded vessel appear, to disappear shortly, and then perhaps to reappear over and over again with further alterations in the state of the systemic circulation. Those who object to such an explanation point out that there may be a lag in the development of symptoms following a drop in systemic blood pressure, or a lag in recovery following the restitution of systemic blood pressure. They point out also, and rightly, that it is not always possible to reproduce symptoms by dropping the blood pressure experimentally. Yet it is not clear that the drop of systolic pressure has been adequate to test the situation. Such objections represent a failure to recognize the multiple factors involved in maintaining the cerebral blood flow in cases of reduced blood pressure. By using the tilt-table technic as a test of insufficiency it is possible to demonstrate that electroencephalographic abnormalities may appear even when clinically evident dysfunction does not (25). Further, it has been shown that once partial infarction has occurred the lessening of tissue demand has relieved the state of insufficiency, and symptoms are no longer easily provoked by any means. This is, in a sense, analogous to the effect of tilting on the electrocardiogram of patients with coronary artery disease (26). Much further work must be done in this area, but the fact remains that, as in the other parts of the circulation, the production and the ultimate result of insufficiency depend largely on the state of the general circulation.

Whatever may be the cause of derangement of the general circulation (hypotension, decreased cardiac output, acute pulmonary edema, alterations in cardiac rhythm) the determining factor at the level of the cerebral circulation is an alteration in the pressure gradient between the collaterals and the area of supply compromised by vascular occlusion. The continuing effectiveness of the collaterals requires that their flow be greater, and if their flow fails because of failure of the general circulation, the gradient is lost, too little blood flows into the compromised area and dysfunction with recovery or infarction

ensues, depending on the duration and intensity of the ischemia.

These considerations of the dynamic factors which underlie vascular insufficiency and infarction of the brain obviously make the problem more complex than the old "plug-and-spasm" school of thought would have us believe. Yet at the same time they permit a more intelligent and more constructive approach, particularly in the treatable stage of the disorder. In patients who present the symptoms and signs of cerebral infarct or cerebral vascular insufficiency and even in those with the background for emboli, the question must be asked, "Why does this patient have this infarct at this time?" Search for and management of an underlying lesion of heart, lung or gastrointestinal tract may reveal abnormalities which are important contributory causes to the pathogenesis of a particular infarct. Of obvious and pressing importance is the exclusion of a myocardial infarct. The experienced physician is able to exclude this possibility in the conscious patient if he can get a proper history and can find no appropriate physical signs. An electrocardiogram should be taken in all patients who have been rendered unconscious by a cerebral infarct.

Diagnosis

Depending on the etiology and the location of an infarct of the brain, the clinical course and the symptoms and signs will vary from case to case. Certain generalizations can be made which aid more precise diagnosis.

Loss of consciousness usually signifies a large lesion. For example, a complete hemiplegia with preservation of consciousness is likely to signify a small, strategically placed capsular lesion, while a complete hemiplegia with unconsciousness is likely to signify that a more complete area of distribution of middle or anterior cerebral artery supply has been infarcted.

Headache is not ordinarily thought of as one of the prodromal signs of infarcts of the brain. Yet headache is relatively common at the onset, especially in certain cases of internal carotid or basilar infarcts. It is never as severe as the headache of intracerebral or subarachnoid hemorrhage and probably is related to the dilatation of the collaterals in their efforts to compensate.

Convulsions at the onset of an acute infarct are not at all common and always should raise the question of another process. When convulsions do occur in acute infarction, they are likely to be the consequence of a diffuse anoxia, such as occurs

in acute occlusion of the internal carotid artery. Convulsive disorder as a consequence of old infarcts is not uncommon—one series places them as high as 26% (27)—and their mechanism in such cases is probably similar to that in the cortical scars of post-traumatic epilepsy.

The mode of onset in an infarct may be sudden, gradual over seconds to minutes or step-like over minutes to hours to days. Most infarcts, and probably all embolic infarcts, declare themselves suddenly. Gradual or step-like development is more likely to mean new occlusion or collateral failure in an insufficient cerebral circulation. From what has been said already about mechanisms it can be understood that there are in the evolution of a lesion no absolutes which allow certitude about the mechanism of infarct production.

Of special interest is the so-called "stuttering onset" of some vascular lesions, especially in the internal carotid distribution. A patient has the sudden onset of a hemiplegia, which remains for several minutes and then clears abruptly and completely. The same hemiplegia with the same recovery then recurs over and over again, sometimes as often as 10 or 20 times in the same day. Finally a hemiplegia occurs from which there is no recovery. Or there may be similar recurrent episodes of failure of monocular vision ("amaurosis fugax"). Such an evolution means a chronic occlusion or severe stenosis of the internal carotid artery. A similar stuttering onset may occur in the vertebral-basilar distribution. Needless to say, not all patients with stuttering course go on inevitably to infarction.

Treatment

The patient with established or impending infarction of the brain should be put to bed. Sometimes beneficial results may be gained by elevating the foot of the bed. From what has already been said, there would seem little reason to administer any vasodilating drugs, since the likelihood is that the tissue metabolites in the damaged area are providing all the stimulation to increased flow which is possible under the circumstances. Some physicians still use papaverine in oral doses of 100-300 mg. or intravenous doses of 30-120 mg., repeated every 3-5 hours and claim good results. We have not been encouraged by our experience with it. Theoretically, there would seem to be less indication for its use the longer the symptoms have been established.

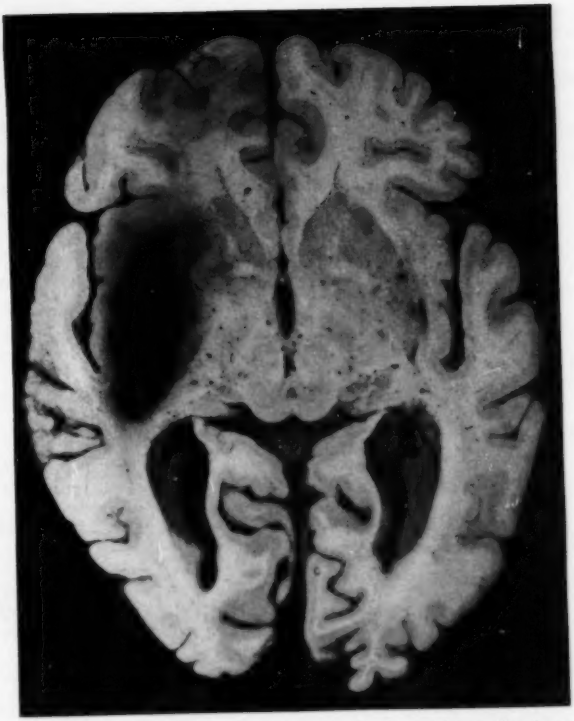

FIG. 2.—Hypertensive hemorrhage in the lateral ganglionic region of the brain.

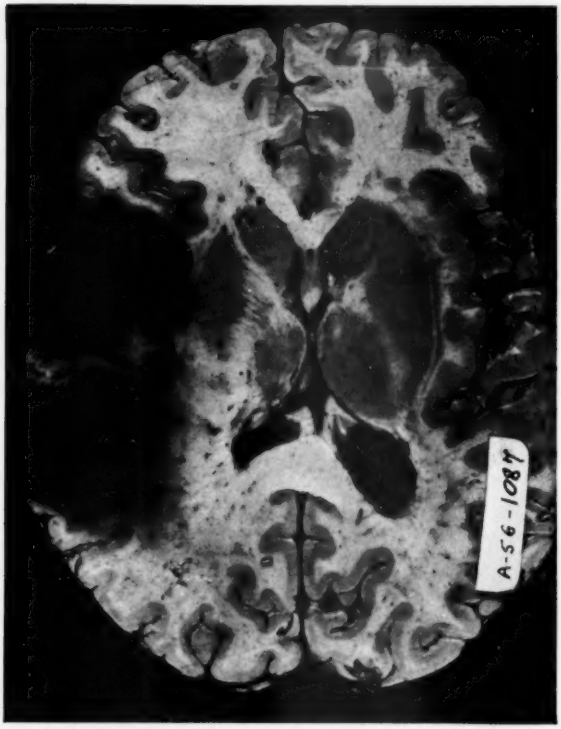

FIG. 3.—Hemorrhagic infarct due to embolic occlusion of the middle cerebral artery.

Stellate ganglion block is still performed by some people but its popularity has waned. We have never seen any evidence that it has had a determining result on the outcome of an infarct. The method is not only irrational but ineffective, and most experienced physicians now regard it as meddlesome.

It has been suggested that cortisone might have some benefit in reducing the swelling and tendency to herniation in some large infarcts (28). The dangers would seem to outweigh the advantages and we have been unwilling to use it. A recent report denies that it has any value (29).

Anticoagulants in cerebral vascular disease have attracted increasing interest in recent years, but their use must still be regarded as experimental. At present the situation in regard to anticoagulants is confused and controversial. It is difficult in an evolving area of therapeutic experimentation to lay down any rules. However, certain points of relative agreement might be stated, which will help point the way:

1. With the possible exception of hypertensive cerebral vascular disease, there does not seem to be any real danger of increasing bleeding in the brain when anticoagulant drugs are used.
2. Anticoagulants have no effect on the evolution or outcome of an established infarct.
3. Their principal alleged effectiveness is in those infarcts which advance by a step-like progression of symptoms and signs, especially in those clinical states in which there are recurrent intermittent episodes of ischemia as a consequence of insufficiency in the internal carotid or basilar artery supply (30).

Thus it would seem clear that the most likely role of anticoagulant drugs in cerebral vascular disease may be in preventing impending infarcts. There are still many reservations about their use. Demonstration of their effectiveness will be largely a statistical problem, since there is an enormous variability in the natural history of threatened infarction. Further, there is some reason to be skeptical of the rationale for their use in the very circumstance in which they seem most effective—the intermittent episodes of dysfunction due to insufficiency. Surely they do not dissolve a clot; and it is difficult to understand how intravascular clotting can be implicated in the patient who has 20 or 30 recurrent episodes over a 2-day period. It well may be that anticoagulant drugs have properties quite apart from their anticoagulant properties.

The technic of administration varies from clinic to clinic.

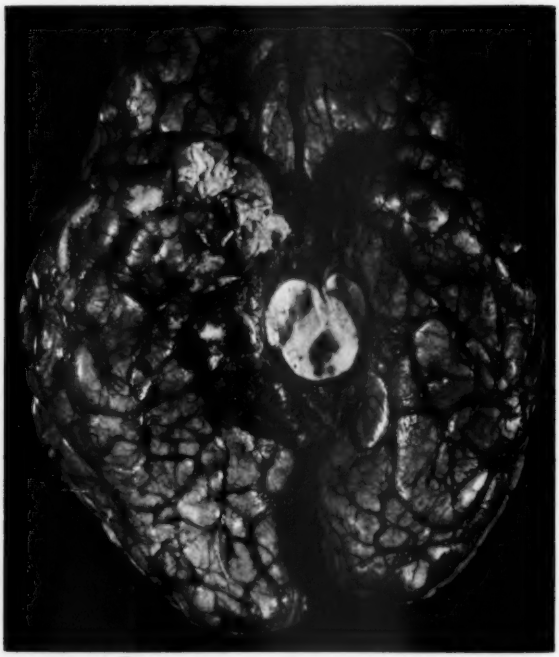

FIG. 4.—Herniation of the right temporal lobe as a consequence of massive infarction of a hemisphere.

Many are now inclined to use heparin in the early stages, following it with Dicumarol® for prolonged administration. Once the anticoagulants have been started, the physician in charge has a lion by the tail. He must keep therapeutic levels and watch for bleeding. Some patients have been continued on the drugs for years. There is no data on when it might be completely safe or wise to stop them. A considerable proportion of patients presenting symptoms of insufficiency cease to have further attacks without the benefit of anticoagulants. The condition has a natural tendency to readjustment if the patient survives the initial phase of repeated attacks. It is therefore extremely doubtful if it is necessary, as some imply, to maintain such patients on anticoagulants for the remainder of their lives.

One of the dangers in experimental methods of management like the use of anticoagulants is that they might depress the physician's alertness to the more obvious alterable factors. A search must be made in the rest of the circulation for any precipitating factors, and especially must cardiac disease be brought under control. In episodes due to insufficiency, as even in the dizzy spells of the elderly, the physician can often detect precipitating causes and modify their influence. Sudden changes in posture, especially from the recumbent to the erect position, may produce an episode, and in such cases the patient can be taught to avoid these sudden changes. Some patients do well with a tight-fitting abdominal support or elastic stockings or both. Overexertion or heavy eating precipitates other attacks. Injudicious use of nitroglycerin in coronary artery disease is responsible for attacks in other cases. The careful physician, the one who pays scrupulous heed to the history and findings and who thinks in physiologic terms about infarction and impending infarction, still has many weapons at his disposal, even if he chooses not to use controversial, cumbersome, potentially hazardous methods.

THE NEUROLOGY OF HYPERTENSION

The effects of hypertensive vascular disease on the cerebral circulation are many and varied. There is a regrettable tendency to equate or confuse them with the effects of arteriosclerotic vascular disease. Although it is true that hypertension is frequently complicated by atherosclerosis of the larger and smaller arteries of the brain, hypertensive cerebral vascular disease presents certain unique problems in pathogenesis, diagnosis and treatment.

The important manifestations of hypertensive cerebral vascular disease are (1) hypertensive encephalopathy, (2) hemorrhage into brain substance, (3) lacunar infarcts and (4) arteriosclerotic aneurysms.

Hypertensive Encephalopathy

Hypertensive encephalopathy is one of the most abused terms in the whole field of cerebral vascular disease. It has been used to describe almost any cerebral event to which the hypertensive may fall victim. In fact, however, hypertensive encephalopathy is a distinct and important specific condition.

Clinically, there is a preceding rapid rise in blood pressure to levels higher than usual for the given patient. Headache, convulsions, stupor going into coma are associated with the fundoscopic manifestations of papilledema, exudates and hemorrhages. Some degree of renal failure is common, but the essential usefulness of the term hypertensive encephalopathy is to cover cerebral disorders that are not adequately explained by "uremia." As a result of repeated attacks the cerebrovascular and renal effects become ultimately associated. In the patient with long-standing hypertension, massive hemorrhage into the brain may complicate or terminate the course. Although many patients die, others recover even without any treatment.

Hypertensive encephalopathy occurs in eclampsia, acute glomerulonephritis, cortisone poisoning, polyarteritis nodosa and other short-term cases of hypertension as well as in the long-standing instances of hypertensive cerebral vascular disease. It can be reproduced experimentally in animals (31). The important change is the rapid elevation of blood pressure, the symptoms and signs most probably resulting from the increased intraluminal pressure of the smaller arteries and arterioles.

Pathologically the impressive gross change is a swelling of the brain. Microscopically, there is edema, high protein fluid or cellular accumulations about blood vessels, depending on the stage of the process. Micro-infarcts and petechial hemorrhages are present. Changes in the walls of the arterioles and smaller arteries depend on whether there has been pre-existing, long-standing hypertension. In addition to the cellular increase and hyalinization of the vessel wall, necrotizing arteriolitis may appear, but it never approaches the degree seen in other organs such as the kidney.

The treatment of hypertensive encephalopathy can be stated

very simply—lowering the blood pressure will relieve the symptoms and signs. How to lower the blood pressure in an individual case calls for a considerable exercise of judgment. The hypertensive patient often has severe complicating atherosclerotic disease of his cerebral arteries. Too rapid reduction of blood pressure may result in reduction of cerebral blood flow generally to produce anoxic encephalopathy, or locally to produce an infarct. In such patients the blood pressure must be lowered more slowly and the patient watched carefully during the reduction. Although the newer hypotensive drugs have undoubted value in the rapid reduction of blood pressure and although they have a splendid usefulness in some cases of hypertensive encephalopathy, their physiologic effect on the cerebral circulation is still largely unknown. In the presence of such high-powered and high-priced medication, one should not lose sight of the fact that there are some patients who do well by being put to bed with mild sedation, or even without it.

Hypertensive Brain Hemorrhage

The most common cause of primary bleeding into brain substance is hypertensive cerebral vascular disease. Unlike hypertensive encephalopathy, brain hemorrhage of any magnitude requires that the hypertension be of relatively long standing and of relative severity. Arteriosclerosis without hypertension cannot produce hemorrhage. Angiomas, blood dyscrasias, trauma and meningocerebral bleeding from ruptured aneurysms are the only other important causes of bleeding into the brain.

The pathogenesis of hypertensive hemorrhage is unknown. In efforts to determine the pathogenesis, a certain amount of confusion has arisen from a failure to differentiate true hemorrhage from hemorrhagic infarction. A hemorrhagic infarct, like other infarcts, is generally in the distribution of a specific blood vessel; a true hemorrhage knows no boundary of vascular supply. In a hemorrhagic infarct, the general architecture of the tissue is preserved and blood is diffused through the tissue; in a true hemorrhage, the architecture is destroyed by the bleeding and blood has destroyed and displaced brain substance. A hemorrhagic infarct results when there is originally an ischemic infarct with restitution of blood flow at a time when the blood vessels in the infarcted area are rendered abnormally permeable by the ischemia. It is for this reason that hemorrhagic infarcts are so common in embolic infarction; the embolus, lodged in the

vessel to produce an ischemic infarct, breaks up and passes into the smaller vessels, allowing the restitution of blood flow (32). It is true that some of the bloodiest of hemorrhagic infarcts may occur in hypertension but even then they need not be confused with true hemorrhage.

The old theory that hemorrhage results from the formation of miliary aneurysms on intracerebral arteries is no longer tenable. The recurrent theory that hemorrhage occurs only in pre-existing areas of infarction fails to take into consideration the specificity of hypertension in the production of hemorrhage, and the much greater frequency of infarcts when compared with hemorrhage. The primary lesion of hypertension in the cerebral arterial tree is in the arterioles and small arteries, which become hyperplastic and hyalinized. Sometimes atheromata appear in these small vessels, but cerebral hemorrhage can occur in the absence of any atheromatous deposits on either small or large arteries. It is likely but far from proved that the essential change in hypertensive hemorrhage relates to the degenerative changes in the smaller branches of the cerebral arterial tree.

The vast majority of hypertensive hemorrhages are in the cerebrum. In a series from our laboratory, 80% were in the cerebrum and roughly 10% each in the pons and cerebellum (33). The symptoms may have an apoplectic suddenness or they may be gradual over a period of several hours. Cerebral hemorrhages begin most frequently in the lateral ganglionic region, less frequently in the thalamus, and infrequently in the white matter. In cerebral hemorrhage, the onset is usually sudden, with a gross hemiplegia and unconsciousness, although a few may have only headache and mild hemiparesis, with aphasia in left hemisphere lesions. Tentorial herniation is usually the rule, and a fatal outcome probably occurs in 90-95% of all cases. Pontine hemorrhage is characterized by violent and rapid collapse, with early pupillary abnormalities and extraocular palsies. Hemorrhage in the pons can produce death within an hour or two, more rapidly than any vascular lesion of the brain, except for massive rupture of an aneurysm. Cerebellar hemorrhage is characterized by intractable vomiting and here, too, death is quick if there is massive rupture into the fourth ventricle.

The diagnosis of hemorrhage in the brain is not difficult. A catastrophic event in a hypertensive patient, with signs of a massive defect in function, and with evidence of meningeal irritation, is the usual clinical picture. It is sometimes difficult to

distinguish from a massive infarction of the brain. The usefulness of lumbar puncture in making the diagnosis will be considered later.

Treatment is usually unavailing. The general measures for care of the acute stage will be considered in a separate section. Reduction of the blood pressure does no good, and may do harm. Not enough experience with induced hypothermia is available on which to form a judgment. In the following situation, surgical intervention may be warranted. When a patient survives the first few critical days, shows some signs of recovery of lost function and then begins to lose function gradually, evacuation of the hematoma by surgery may be indicated. This is especially true if there is increasing papilledema. In such cases, the hematoma acts as an expanding lesion by picking up fluid, and evacuation may produce a dramatic result. However, such cases are rare, and no more than one or two a year are seen in a large general hospital.

Lacunar Infarcts

The predilection of hypertension for the small blood vessels of the brain results in the production of tiny infarcts of a few millimeters in diameter. These are especially prone to occur in the lenticular nucleus, the base of the pons and in the central white matter of the hemispheres. They are responsible by their cumulative effect for the frequency of gait disturbances, pseudobulbar palsy and dementia in hypertensive patients who show no clinical evidence of gross lesions in the brain.

Lacunar infarcts occur in hypertension more than in any other state. Uncomplicated arteriosclerosis does not produce them, but they may occasionally be seen in nonhypertensive diabetics and very elderly people.

Arteriosclerotic Aneurysms

Long standing hypertension has the effect of producing tortuosity of the vessels of the circle of Willis and their branches. This effect is best seen in the tortuous elongation of the vertebral-basilar system. When this effect is combined with the effects of severe atheromatous degeneration of the vessel wall, the result is fusiform aneurysmal dilatation. Such deformity reduces the effectiveness of the vessel, transforming it into an inelastic

tube, and sometimes narrowing the ostia of the branches. Hemorrhage from such aneurysms is rare, although we have seen one massive subarachnoid hemorrhage from rupture of an arteriosclerotic basilar aneurysm and one carotid-cavernous fistula with exophthalmos from rupture of an arteriosclerotic carotid aneurysm.

More important are the effects of such lesions on adjacent cranial nerves (34). In the carotid system, the compression of the optic nerves does not often produce clinical effects. In the vertebral-basilar system, however, the vessels may run obliquely into the cerebellopontile angle, and then indent the pons in their oblique course in the opposite direction. In the angle, there may be compression of the 8th nerve to produce deafness, of the 7th nerve to produce facial spasm or of the 5th nerve to produce facial pain.

ANEURYSMS

Congenital aneurysms are saccular deformities of cerebral vessels which manifest their presence by compression of the brain or cranial nerves, by bleeding into the subarachnoid space (spontaneous subarachnoid hemorrhage), into the brain (meningocerebral hemorrhage), or into a venous sinus with the production of an arteriovenous fistula. They are also referred to as "berry aneurysms." These aneurysms occur at the branching of cerebral vessels, and almost all are found at or near the circle of Willis. While an aneurysm may remain silent until the 7th or 8th decade, or may give symptoms at the end of the 1st decade, clinical complaints generally occur in the 3d, 4th or 5th decades.

Spontaneous subarachnoid hemorrhage occurs classically as an episode without prior warning in a young normotensive person and is characterized by collapse, headache, signs of meningeal irritation, paralysis of cranial nerves, usually the 3d and grossly bloody cerebrospinal fluid under increased pressure.

The diagnosis of rupture is unlikely to be confused with other neurologic disorder. The patient has the abrupt onset of a severe headache in the occipital region, which he often describes as "the worst headache I have ever had." Regrettably, sexual intercourse is a frequent precipitating exertion. This headache then becomes generalized, and nausea and vomiting commonly appear. Stiff neck and positive Kernig's sign appear early. The patient may fall unconscious shortly after the onset and some

patients may die within a few minutes. Other patients may become confused and agitated, and sedation becomes necessary. Simple subarachnoid hemorrhage generally is not associated with severe lateralizing neurologic signs. If asymmetric brain swelling occurs there may be increase in tendon reflexes on one side or pupillary asymmetry. Diffuse brain swelling may produce varying degrees of coma, bilateral extensor plantar reflexes and even decerebrate rigidity. If the aneurysm is adjacent to the oculomotor nerve, complete or incomplete third nerve palsy may occur. The mortality reported for the first day in spontaneous subarachnoid hemorrhage ranges from 15% (35) to 23% (36). By the end of the 3d week approximately 40-50% of the patients have died. Of the causes of death rebleeding is the most important. One of the consequences of rebleeding, or indeed of the original episode, is meningocerebral hemorrhage with destruction of a large area of brain and the formation of an intracerebral hematoma.

In a certain number of meningocerebral hemorrhages there is rupture through brain substance into the lateral or third ventricles.

Most of the mortalities in ruptured aneurysms occur in the first 24 hours (60% of Magladery's). Recurrences after the end of the 3d week are less common but 20% of Hyland's (37) patients died of a second episode more than 4 weeks after the first attack. The average expectancy of this group, as a whole, was 6 years. Norlén and Olivecrona (38) reported that in 18 nonoperated patients with verified saccular aneurysm who survived the initial bleeding, 5 died within 3 years, 2 others died of unknown disorders, 2 were unreported and 9 were alive up to 9 years. Of these, 1 had persistent ophthalmoplegia, 1 a new attack of ophthalmoplegia and 1 was disabled because of mental disorder. Factors modifying recurrence are age, hypertension and arteriosclerosis. Thus, in Magladery's study the mortality in normotensive persons under age 60 was 29%, in contrast to 46% for his total group. The site of the catastrophe, its size, the presence of extracerebral or intracerebral clot and the degree of cerebral edema all affect survival after a single attack.

The management of aneurysmal rupture constitutes one of the knottiest problems confronting the physician, for not only must treatment be directed toward immediate survival but also toward prevention of future attacks. Magladery (36) has recently stated that his clinical material "does not support the view that presently available surgical means of intervention

offer any improvement over the current conservative approach." In his group the surgical mortality was 56%. In sharp contrast, however, is the recent work of Botterell (39) who reported on 22 cases in which the aneurysm was approached directly with induced hypothermia and the interruption of carotid and vertebral circulation under EKG and EEG control. Three patients died, and 19 recovered, 16 with excellent, 1 with fair and 2 with bad results.

On the basis of presently available information, it would seem that Botterell's technic offers patients the greatest opportunity for survival and cure. It would seem that treatment, to be effective, must select the patient under 60 who has normal blood pressure, who does not have a profound meningocerebral hemorrhage and who is not decerebrate. We believe that arteriography should be done early, if possible under local anesthesia, and should be bilateral, since 20% of patients have more than one aneurysm. Operation should be directed toward the aneurysm itself since carotid ligation may not only obliterate the aneurysm but also may risk carotid insufficiency later in life. The patient over 60, or the severely hypertensive patient, presents an entirely different problem and we believe that he is usually best handled by nonoperative methods. Arteriography in this group carries a somewhat higher risk than in the younger normotensive group. Complications of this procedure occur in about 3% of all cases and can be reduced by patient selection, use of local anesthesia, use of minimal amounts of contrast medium and pretesting for sensitivity. Arteriography will demonstrate aneurysm or other malformations of cerebral vessels in about 50% of cases.

Those patients treated conservatively and all patients preoperatively require the same sort of nursing care referred to under Management of Stroke (p. 36), but with special attention to respiratory needs. They may need frequent suctioning or even tracheotomy. In general, respiratory failure treated by mechanical respiration of any type only defers a fatal outcome for a few hours. We advocate absolute bed rest for 2-6 weeks. Visiting should be kept at a minimum and the patient fed and bathed by nurses in the critical postbleeding period.

Regardless of the form of therapy, a patient with an established complete 3d nerve palsy does not recover completely and some degree of neurologic deficit always remains after meningocerebral bleeding or cerebral infarction.

Survival after 3 subarachnoid hemorrhages usually indicates

another type of vascular malformation, i.e., angioma. These often are associated with bruit audible both to patient and physician. The bruit is variable in its occurrence and is rarely heard by the physician unless the patient hears it as well. Most of these lesions are identifiable on plain x-ray as a honeycombed or railroad track pattern of calcification. Many fill from more than one cerebral vessel. The ideal case for surgical attack is one in which the angioma is filled by a single vessel and one in which the location of the malformation is not such that removal or damage to nearby tissue produces a severe neurologic deficit.

Survival beyond 10 years is the expectation in patients with angioma, although there may be convulsive disorder or focal brain damage from hemorrhage.

VENOUS DISEASE

Regardless of the etiology, cortical thrombophlebitis produces 3 categories of symptoms and signs: (1) those due to increased intracranial pressure and cerebral edema, (2) focal convulsions and (3) those defects resulting from venous infarction of the brain. The process may involve but a single cortical vein or it may involve a major venous sinus. When the latter obtains, the symptoms and signs of deficit are more diffuse and indeed may alternate from side to side.

While some cases of venous occlusion are associated with malnutrition, carcinomatosis, collagen disease and vascular malformation, most derive directly or indirectly from infectious disorders.

Those that derive directly from infectious disorders consist of: (1) thrombophlebitis of the lateral or transverse sinus secondary to suppurative middle ear disease, (2) thrombophlebitis of a cortical vein, usually frontal or precentral, secondary to subdural or epidural empyema, osteomyelitis of frontal or ethmoid sinus and (3) thrombophlebitis of the cavernous sinus resulting from extension of petrosal sinus thrombophlebitis or thrombophlebitis of a facial vein.

Those that derive indirectly occur in association with severe wasting and generalized infection and are not properly included here. The clinical and pathologic evidence supporting metastatic infection to cortical veins via Batson's vertebral plexus is insufficient to justify a discussion here.

Thrombophlebitis of the lateral or transverse sinus is charac-

terized by head pain and retroauricular and neck pain. The skin and emissary veins behind the ear may appear congested. The intracranial pressure is usually elevated and the cerebrospinal fluid usually contains some white cells. Protein is increased but sugar is normal. The patient may be confused and have contralateral seizures and mild contralateral weakness.

Infective thrombosis of a cortical vein usually produces sharply focal contralateral neurologic signs with focal seizures. Since this often occurs in association with subdural or epidural empyema, the cerebrospinal fluid is under markedly increased pressure with a large number of cells and elevated protein, but no microorganisms and normal sugar. This disorder may occur as a consequence of more general disease of cerebral veins with occlusion of the sagittal sinus. In this instance, the focal signs alternate from side to side and the signs of elevated intracranial pressure are more prominent.

In some instances, thrombosis of the lateral sinus involves lesser sinuses as well, e.g., the superior or inferior petrosal or, conversely, focal purulent disease may involve these sinuses primarily. Such thrombophlebitis of the lateral sinus produces a sharply focal faciobrachial monoplegia on the side opposite the lesion. On the major side this may be associated with aphasia. Thrombophlebitis of either petrosal sinus causes focal cranial nerve compression, especially of the 6th.

Thrombophlebitis of the cavernous sinus usually proceeds from direct extension of thrombophlebitis in a facial vein. At first, one cavernous sinus is affected, and by way of the anastomotic circular sinus the other shortly becomes involved. Septic obstruction of the cavernous sinus produces the unforgettable and terrifying state of a confused patient with papilledema, peripapillary hemorrhages, blindness, edema of the lids, forehead and "butterfly" area of face. The small veins along the root of the nose and upper lids are engorged. There is exophthalmos and palsy of the nerves to the eye muscles. Because the first division of the 5th nerve may be involved, there often is pain and altered sensation in the forehead and cornea. The cerebrospinal fluid pressure is extremely high. Thrombophlebitis of this sort may be a source of septicemia and septic pulmonary embolization.

The treatment depends on the underlying disorder, i.e., surgical drainage of the source of the infection and appropriate antibiotics. If the patient survives, he generally recovers satisfactorily except in the instances of cortical thrombophlebitis

where a nicely recovered hemiplegia may be associated with postphlebitic epilepsy, of the same pathogenesis as post-traumatic epilepsy.

LUMBAR PUNCTURE IN CEREBRAL VASCULAR DISEASE

The point of view that lumbar puncture is essential in all cases is as erroneous as the point of view that it is necessary in none. Indiscriminate use of lumbar puncture is to be deplored, because both hemorrhage and large infarcts of the brain can produce swelling of sufficient intensity to produce herniation through the tentorial opening or through the foramen magnum.

If there is a clear history of the sudden onset of a gross deficit of brain function in a patient whose general condition gives reason to believe that he has a disease of cerebral blood vessels and no evidence of sepsis, lumbar puncture is not likely to yield any information which will change the physician's approach to the problem. The distinction between infarct and hemorrhage can usually be made on clinical grounds. On the other hand, if there is any suggestion of sepsis, or if the history is not clear-cut, a lumbar puncture is a necessity. When it is done, it should be done with the same scrupulous care which is exercised when an expanding lesion is suspected. This means a small-gauge needle, proper measurement of pressure *without the Queckenstedt test,* and gradual withdrawal of no more than the few cc. necessary for the determinations.

In subarachnoid hemorrhage, especially with focal neurologic signs, the decision regarding lumbar puncture must be made just as critically. The classic history of a sudden, severe, violent headache with prostration, nausea, vomiting and signs of meningeal irritation is as diagnostic of subarachnoid hemorrhage as is a manometer full of blood.

The findings on lumbar puncture must be interpreted critically. Generally, in infarcts, there are no cells and a normal protein finding. However, in some larger infarcts, at the 3d or 4th day of their evolution, large numbers of white blood cells may appear in the fluid to simulate an infectious reaction. In some infarcts, also, the protein may rise to 60-100 mg./100 ml. The physician must view the total situation and avoid the panicky tendency to rush into a group of unnecessary and sometimes dangerous diagnostic procedures. It should be emphasized particularly that pneumoencephalography and arteriography

are most likely to produce trouble in the presence of severe hypertensive or arteriosclerotic vascular disease.

The "bloody tap" is always a troublesome finding and, unless properly interpreted, may confuse the whole clinical problem. When bloody fluid is withdrawn, the decision about the origin of the blood is best made by two methods. The red cells should be counted in the first and in the third tubes used for collecting. If there is a significant difference in the number of red cells (either an increase or a decrease) the likelihood is that the bleeding is coming from the site of the needle puncture. A helpful supplemental method is to spin the red cells down immediately in a centrifuge. If the supernatant fluid is colorless or has only a trace of xanthochromia, the likelihood is that the bleeding was produced by the needle. The supernatant fluid in cases of subarachnoid hemorrhage of any cause should be quite strongly xanthochromic. Crenation of red cells is a poor method of differentiating a traumatic tap from true intracranial bleeding. Generally speaking, it is dangerous to diagnose subarachnoid hemorrhage unless the red cells are in excess of 15-20,000/-cu. mm. Indeed, most often they number hundreds of thousands.

Since syphilis can produce cerebrovascular disease, the progression of which can be arrested by therapy, a serologic test for syphilis must be undertaken on every spinal fluid. A positive serologic test for syphilis is, of course, not diagnostic of active neurosyphilis. Indeed, in the presence of increased red or white cells or protein due to the stroke, a positive reaction in the cerebrospinal fluid may represent only a transient and clinically insignificant passage of reagin from positive blood into the cerebrospinal fluid.

MANAGEMENT OF STROKE

Regardless of the cause of the stroke, the basic principles of treatment remain the same. In general, the management problem can be divided into two groups, those directed toward the patient's survival and those directed toward restoration of the patient's economic and social function. Measures aimed at achieving both these objectives begin with the onset of the stroke, and if either is neglected much valuable time may be lost.

Since all such illnesses develop against a background of some systemic illness, e.g., hypertension, arteriosclerosis, diabetes, syphilis, etc., an effort should be made to uncover the substrate

in which the stroke has occurred. Ideally, patients should have the following studies: hemoglobin, hematocrit, sedimentation rate, white blood count, differential, urinalysis, nonprotein nitrogen, blood sugar, serologic test for syphilis and x-rays of chest and skull. Since early lumbar puncture may produce a risk of herniation, it should be deferred generally until the patient is clearly beyond the danger of herniation, and then its objective should be only to discover a treatable underlying cause, such as neurosyphilis. Electrocardiograms should be made, but electroencephalograms add little to the understanding or management of the acute episode in most cases. The temperature, blood pressure and pulse should be observed frequently and regularly. In the event of persistent fever, cultures of blood, urine and sputum should be made. Prophylactic antibiotics do not prevent infectious complications and we believe that patients do less well on these agents than when antibiotics are withheld to await a specific complication.

The conscious patient who swallows well rarely has respiratory difficulty but the patient with dysphagia is endangered by aspiration and must be protected by oropharyngeal aspiration. Frequently the patient can be taught to do this for himself. The comatose patient in addition to being endangered by aspiration, needs protection against atelectasis. This may be achieved by turning him from the prone to the lateral to the supine position on a regular schedule, ideally every half hour. As the patient recovers his ability to swallow he can usually handle viscous liquids, e.g., gelatin, custard, porridge. Later, he is able to handle most foods but usually is left with residual difficulty with thin liquids such as water.

The use of oxygen does not usually benefit the patient who is breathing well and has good color. Before using oxygen, one must be certain that the respiratory difficulty is not the result of obstruction either at a high level or in a main bronchus.

Patients rarely need vasopressor or vasodepressor substances. We do not believe that efforts to lower blood pressure are of value, and indeed they may be harmful. It has been our experience that a relative hypotension for a given hypertensive patient may be a greater hazard than the hypertension. Efforts at maintaining cardiac output are often helpful. Postural stimulation of blood pressure by lowering the head has been most effective. Elastic stockings not only prevent phlebothrombosis, but also prevent loss of fluid into interstitial spaces, especially in the paretic leg. The patient who has lost all or part of the use

of one side of the body is often intolerant to being erect. When ambulation is first attempted one must guard against postural hypotension.

A stuporous, sweating, elderly hemiplegic, head hanging forward, tongue hanging out, drooling, strapped to a chair, cannot be considered on the way to ambulation, and is better off in bed.

Renal problems per se rarely arise as long as cardiac output, blood pressure and hydration are maintained. An indwelling catheter often leads to hemorrhagic cystitis and this is almost invariable in the diabetic. In male patients a urinal can usually be propped between the thighs, and the patient kept dry in this way. The problem is rather more difficult in the female patient especially when she is obese, but usually an ordinary urinal can be used here too.

The slender patient, or the obese one who is likely to remain in bed for a long time, requires particular skin care. Such patients should be on a foam rubber mattress, turned systematically from side to side and kept dry. A common nursing error is in dragging rather than turning the patient on sheeting. Decubiti are best treated by keeping the lesion dry and exposed to the air. Soaks or ointments lead to further maceration of the skin by reproducing the very circumstances which produce the sore.

Convulsive disorders rarely complicate acute strokes, although there may be a few, especially at the onset of embolic brain disease. Phenobarbital, 60-100 mg. subcutaneously at 3-4 hour intervals, usually suffices to handle this problem. For longer-term medication either this drug or sodium diphenylhydantoin may be used. If the latter is chosen, the capsule should be avoided, since it may prove difficult to swallow and may dissolve in the mouth, producing a disagreeable bitterness. This drug is supplied in a pleasant sirup.

The long-term goals in the patient with a stroke are twofold: employment and enjoyment. The most important complication of immobilization and the principal obstruction to attainment of these goals is joint contracture. The great joints, hip and shoulder, are most readily affected but the fingers, wrist and ankle may also be involved. From the day of onset, careful passive manipulation should be instituted with each involved joint passed through a full range of motion at least 10 times, 3 times a day. Abnormal postures, e.g., finger flexion and foot drop, should be counteracted by the use of night splints to the hand

and ankle. The leg is often more comfortable if the knee is slightly bent. It is well to remember that the hand movement most often lost is that which opens the hand. Too great concentration on the movement of flexion, as in squeezing a ball, is illogical when the weakness is in dorsiflexion of wrist and fingers. If contracture has developed, it too can be dealt with by passive manipulation but if the patient is capable of any movement he should be encouraged to make the movement with the physiotherapist. Joint manipulation should be gentle and careful lest it result in joint trauma and permanent fixation.

There is no rule regarding ambulation. As soon as the patient has stabilized in regard to vital signs, is conscious and is able to maintain his head erect, he should be gotten out of bed. This generally requires but a day or two. When the patient is first up in a chair, hypotension may be prevented by the use of elastic stockings and an abdominal binder and the blood pressure should be checked frequently during these first efforts. The easiest way to prevent postural syncope is by stimulating the patient to talk or move. This is a convenient time in which to perform joint manipulation. If the arm is flail, it should be supported in a sling lest the shoulder capsule be torn by the weight of the arm itself. At a point where the patient is able to sit comfortably for 30 minutes, walking can be attempted with a long leg brace if necessary. This may be required for only a few weeks but its use materially reduces the period of immobilization and hastens functional recovery. The leg brace usually requires a knee-lock and a T-strap. The latter is used to overcome pes cavus. At first, the patient will require support in walking but later is able to walk with a cane or behind a chair or walking frame. A super-market cart with a 25-pound weight on the bottom shelf is a good substitute for the latter. While the arm and hand usually do less well than the leg, most patients with a slight degree of flexion function in the hand will be able to use a cup and silverware if those provided have large plastic or wooden handles. Many patients will be able to cut their own food if provided with a sharp, stout paring knife.

The patient should be taught to rise from a chair. At first a high chair or an ordinary chair mounted on blocks may be used. The patient should slide forward to place his hip extensors at the greatest mechanical advantage and assist with his arm in rising. The reverse is used in sitting. Moving in bed may be facilitated by a knotted ½-inch rope looped over the foot rail. Efforts should be made to get the patient to care for his own

toilet needs as far as possible. Many will be unable to dress themselves thereafter, but suspenders in place of belts, and snaps in place of buttons help greatly to overcome this problem. Elastic shoe laces which do not require untying once tied convert most shoes into readily donned slippers. Most women remain unable to fasten girdles and brassieres. Shirts, coats and jackets should be put on with the paretic limb first, and even the very spastic patient can be trained to maintain his arm in extension at his side while the sleeve is put on.

Walking and all other aspects of rehabilitation are facilitated by loss of excess weight. After the acute phase of the illness, weight reduction should be effected. The neurologist's enthusiasm for weight loss in the uncomplicated hypertensive or diabetic arises from the knowledge that when the stroke occurs, the obesity may determine the degree of functional outcome.

Speech therapy in the elderly aphasic group is only rarely rewarding, and for all practical purposes more good can be accomplished by teaching the family to adapt to the patient's problems and needs.

All manner of active enjoyment within capacity should be offered patients. Many are capable of reading, weaving, gardening, etc. All of this makes more pleasant a life limited in its range of activity. Complete dependency on others may be the great tragedy for the patient who has had a stroke. Methods should be explored to give the patient whatever responsibility for himself and others his physical situation will permit. The ideal situation is one in which to some measure others are made dependent on the patient.

A word should be said about what is meant by physiotherapy. Three brief periods a week with a most expert graduate physiotherapist are far less valuable than 3 periods a day with an intelligent and ingenious member of the patient's own family. In such situations, the role of the trained physiotherapist is most often that of indoctrinating properly the people who are going to be with the patient all the time.

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